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A PRELIMINARY TOXICOLOGICAL EVALUATION OF EIGHT  
CHEMICALS USED AS WOOD PRESERVATIVES(U) ARMY MEDICAL  
BIOENGINEERING RESEARCH AND DEVELOPMENT LAB FORT.  
J C DACRE MAY 84 USAMBRDL-TR-8405

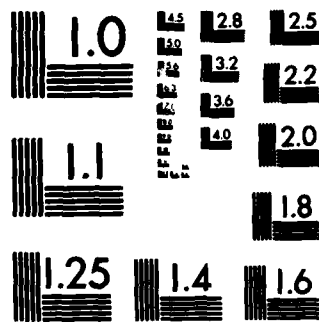
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TECHNICAL REPORT 8405

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A PRELIMINARY TOXICOLOGICAL EVALUATION OF EIGHT CHEMICALS  
USED AS WOOD PRESERVATIVES

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<table border="0"> <tbody> <tr> <td>2-(Thiocyanomethylthio)benzothiazole</td> <td>Ecological effects</td> </tr> <tr> <td>3-Iodo-2-propynyl butylcarbamate</td> <td>Environmental effects</td> </tr> <tr> <td>Ammoniacal copper borate</td> <td>Environmental standards</td> </tr> <tr> <td>Copper 8-quinolinolate</td> <td>Mammalian toxicity</td> </tr> <tr> <td>Copper naphthenate</td> <td>Pentachlorophenol</td> </tr> </tbody> </table>			2-(Thiocyanomethylthio)benzothiazole	Ecological effects	3-Iodo-2-propynyl butylcarbamate	Environmental effects	Ammoniacal copper borate	Environmental standards	Copper 8-quinolinolate	Mammalian toxicity	Copper naphthenate	Pentachlorophenol
2-(Thiocyanomethylthio)benzothiazole	Ecological effects											
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Ammoniacal copper borate	Environmental standards											
Copper 8-quinolinolate	Mammalian toxicity											
Copper naphthenate	Pentachlorophenol											
20. ABSTRACT (Continue on reverse side if necessary and identify by block number)												
<p>A preliminary toxicological evaluation of eight chemicals used as wood preservatives has been made and the data gaps identified. The mammalian toxicology, environmental and ecological effects, and environmental standards for pentachlorophenol, copper naphthenate, copper 8-quinolinolate, 3-iodo-2-propynyl butylcarbamate, 2-(thiocyanomethylthio)benzothiazole, zinc naphthenate, ammoniacal copper borate, and tri-n-butyltin oxide have been reviewed, and recommendations made for further toxicological studies.</p>												

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19. Key Words (continued)

Tri-n-butyltin oxide

Wood preservatives

Zinc naphthenate

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## INTRODUCTION

A request has been received from the Chief, Munitions Systems Division, Large Caliber Weapons Systems Laboratory (LCWSL), ARRADCOM, Dover, NJ, through HQDA, to provide health and environment hazards data for eight candidate alternative wood preservative compounds.<sup>1</sup>

In January 1981, the Environmental Protection Agency issued Position Document No. 2/3 on the wood uses of the three wood preservative pesticides, creosote, pentachlorophenol (PCP), and the inorganic arsenicals.<sup>2</sup> This document proposes several regulatory actions to reduce the human health risks resulting from registered wood preservative uses of these compounds. The proposed actions are based on the Agency's determination that these uses may result in unreasonable adverse effects; for PCP and its salts (or its contaminants), the effects are potential oncogenicity, fetotoxicity, and teratogenicity.

Because of these proposed actions on PCP, the US Army will not be able to continue using this compound to treat all its wood products, e.g., ammunition boxes and tent pegs. Seven other wood preservative compounds have been proposed as candidate chemicals to replace PCP, and it is these compounds that are the subject of this report. The common name, chemical abstract name, accepted abbreviation, and structure of the eight wood preservatives are listed in Table 1.

In order to identify these compounds and to provide access to information in secondary sources, the CAS Registry Numbers and Toxic Substances List Numbers are given in Table 2.



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TABLE 1. LIST OF WOOD PRESERVATIVES

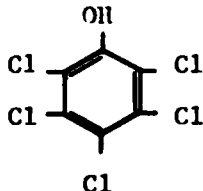
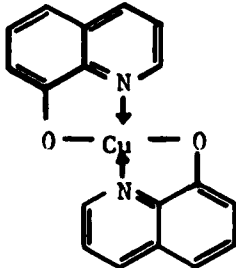

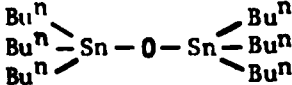
Names	Abbreviation	Formula
Pentachlorophenol (phenol, 2,3,4,5,6-pentachloro-)	PCP	
Copper naphthenate (naphthenic acid, copper salt)	--	
Copper 8-quinolinolate (8-quinolinol, copper(II) chelate)	Cu-8	
3-Iodo-2-propynyl butylcarbamate (carbamic acid, butyl-, 3-iodo-2-propynyl ester)	--	$I-C \equiv C-CH_2O-CO-NH-Bu$
2-(Thiocyanomethylthio) benzothiazole (thiocyanic acid, 2-(benzo- thiazolythio)methyl ester)	TCMTB	
Zinc naphthenate (naphthenic acid, zinc salt)	--	
Ammoniacal copper borate	--	$[CuO:B_2O_3]NH_3$ 2:1
Tri-n-butyltin oxide Bis(tri-n-butyltin) oxide (distannoxane, hexabutyl-)	TBTO	

TABLE 2. SUMMARY OF REGISTRY IDENTIFICATIONS

Compound	CAS Registry No.	Toxic Substances List No.
Pentachlorophenol	87-86-5	SM6300000
Copper naphthenate	1338-02-9	QK9100000
Copper 8-quinolinolate	10380-28-6	VCS250000
3-Iodo-2-propynyl butylcarbamate	55406-53-6	--
2-(Thiocyanomethylthio) benzothiazole	21564-17-0	XK8150000
Zinc naphthenate	12001-85-3	QK9275000
Ammoniacal copper borate	--	--
Tri-n-butyltin oxide	56-35-9	JN8750000

## INFORMATION SOURCES

The three information sources used and the data base search terms are listed here.

### 1. Reference texts:

The following texts were consulted:

- a. Registry of Toxic Effects of Chemical Substances, 1979 Edition. Vols. 1 and 2. 1980. R.J. Lewis, Sr. and R.L. Tatken, eds. DHHS (NIOSH) Publication No. 80-111.
- b. Industrial Hygiene and Toxicology. Vol. 2, Toxicology. 1963. F.A. Patty, D.W. Fassett, and D.D. Irish, eds. 2nd Edition.
- c. Hartwell, J.L. 1951-1980. Survey of compounds which have been tested for carcinogenic activity. Seven volumes + 2 supplements. PHS Publication No. 149.
- d. Handbook of Toxicology. Vol. 3, Insecticides, 1959. Vol. 5, Fungicides, 1959. NAS/NRC.

### 2. Abstract journal searched: Chemical Abstracts to December 1980.

### 3. Computer searches:

The following data bases were searched:

Medline (1966-present)  
Toxline, Toxback (1965-1974)  
CA Search (1967-present)  
Enviroline (1971-present)  
Excerpta Medica (1974-present)  
Oceanic Abstracts, Pollution Abstracts  
Bios Previews (1969-1976), Bios (1977-present)

The data bases at the Environmental Mutagen Information Center and the Environmental Teratology Information Center were also searched.

The data bases were searched using the following terms:

#### Mammalian toxicology:

Human exposure  
Experimental animals  
Biochemistry, metabolism  
Acute, subacute, chronic toxicity  
Eye and skin irritation, skin sensitization  
Carcinogenicity, oncogenicity  
Mutagenicity (Ames), teratogenicity  
Reproduction

#### Environmental Considerations:

Toxicity in other mammals, birds, fish, reptiles, amphibia, insects,  
microorganisms  
Behavior in soil, water, air  
Food chain, plants

#### Standards and Criteria:

TLV, air, water, soil

Because of the short time limit to prepare this report, no claim is made that the literature has been adequately reviewed. Many publications (hard copy) have not been retrieved and many have been reviewed in abstract form only.

#### SUMMARY OF FINDINGS

The findings from this study are presented in detail for each wood preservative in Appendixes A through H. The mammalian toxicology and environmental considerations for each of the eight wood preservatives are summarized below.

##### 1. Pentachlorophenol

Complete and extensive toxicological studies have been carried out on PCP. The potential oncogenicity of PCP is the real cause of concern; it is the presence of two highly carcinogenic impurities, hexachlorodibenzo-p-dioxin and hexachlorobenzene, in the commercial preparations of PCP. Because of this, four studies of PCP (purified PCP, technical PCP, "Dowicide EC-7," "DP-2") have been initiated in the NTP/NCI Carcinogen Bioassay Program.<sup>3</sup> PCP has also been shown to be fetotoxic and teratogenic in animal studies.

##### 2. Copper Naphthenate

The lowest lethal oral dose for copper naphthenate in the mouse is 110 mg/kg, and it has been reported to be an irritant to human skin.

##### 3. Copper 8-quinolinolate

The reported acute toxicity values for Cu-8 in the mouse would indicate that this compound is not acutely toxic. However, there is some evidence that it may be carcinogenic in mice.

##### 4. 3-Iodo-2-propynyl Butylcarbamate

No information was retrieved for this compound.

##### 5. 2-(Thiocyanomethylthio)benzothiazole

The oral LD<sub>50</sub> of TCMTB for rats is 1.59 g/kg; it was positive when tested by the Ames bioassay screen. TL<sub>m</sub> values from 0.15 to >100 ppm have been

reported for a range of aquatic species. TCMTB has some effect on the microfungal populations and some biochemical properties of soil.

#### 6. Zinc Naphthenate

The oral LD<sub>50</sub> for zinc naphthenate in the rat is 4.92 g/kg, and like copper naphthenate, it has been reported to be an irritant to human skin.

#### 7. Ammoniacal Copper Borate

No information was retrieved for this compound.

#### 8. Tri-n-butyltin Oxide

Extensive acute toxicity studies have been reported for TBTO, and the data indicate that it is a moderately toxic compound. It has also been shown to be a primary eye and skin irritant in both man and experimental animals. There is also some evidence from a mutagenic study and a subchronic study that TBTO may be a potential carcinogen.

### DATA GAPS

Much of the information necessary for an evaluation of the health and environmental hazards of these seven substances was not retrieved from the literature. These data gaps are discussed below.

#### 1. Mammalian Toxicology

Very limited mammalian (human and animal) toxicity data exist for the seven compounds reviewed. Extensive toxicological studies have, however, been carried out on PCP. Table 3 summarizes the data retrieved for toxicological properties of these wood preservatives.

#### 2. Environmental and Ecological Effects

There is almost no information available concerning the toxicity of these compounds to aquatic biota (algae, invertebrates, and fishes). The aquatic toxicity data, mainly in fish, are summarized in Table 3. The phytotoxic and possible bioaccumulation properties of these wood preservatives in common native plants grown in contaminated soil are not known. Bioaccumulation has obviously not been studied.

The environmental fates of these wood preservatives are largely unknown; the extent of microbial metabolism is poorly documented. Thus, the extent of their degradation in the environment and the identities of possible stable metabolites are unknown.

#### 3. Environmental Standards

With the exception of PCP, for which a TLV was set at 0.5 mg/m<sup>3</sup> for skin exposures, none of the compounds has been evaluated for the setting of criteria or standard exposure values. NIOSH, however, has reviewed all the organotin compounds, including TBTO, and has recommended an occupational standard of 0.1 mg/m<sup>3</sup> (as tin) for this group of compounds.<sup>4</sup>

TABLE 3. MAMMALIAN AND AQUATIC TOXICOLOGY DATA AVAILABLE

Compounds	Penta-chloro-phenol	Copper naphthenate	Copper 8-quinolinate	3-Iodo-2-propynyl butyl carbamate	2(Thiocyano-methylthio benzothiazole	Zinc naphthenate	Ama. copper borate	Tri-n-butyltin oxide
Acute Oral LD <sub>50</sub> (rats/mice)	+ <sup>a</sup>	± <sup>b</sup>	+M	-C	+R	+R	-	+
Acute dermal LD <sub>50</sub> (rats/rabbits)	-	-	-	-	-	-	-	+
Eye and skin irritation (rabbits)	+	-	-	-	-	-	-	+
Skin sensitization (guinea pigs)	+	-	-	-	-	-	-	+
Mutagenesis (microbes)	+	-	+	-	+	-	-	±?
Toxicokinetics (various animals <sup>e</sup> )	+	-	-	-	-	-	-	-
30 to 90-Day feeding in rats and mice	-	-	-	-	-	-	-	+
1 to 2-Year feeding in rats and mice <sup>f</sup>	+	-	+	-	-	-	-	-
Reproduction (rats)	+	-	-	-	-	-	-	-
Teratology (rats/rabbits)	+	-	-	-	-	-	-	-
Metabolism in various animals <sup>g</sup>	+	-	-	-	-	-	-	-
Aquatic Toxicity	+	-	-	-	+	-	-	+

a. + = Sufficient information retrieved.

b. ± = Information marginally adequate.

c. - = No information retrieved.

d. Ames test, including activation.

e. Metabolism will include absorption, distribution, excretion, and pharmacokinetics, using radio-labeled material.

f. This will include a carcinogenicity evaluation.

g. This will include the identification and possible isolation of any metabolites.

## RECOMMENDATIONS

It is quite clear from Table 3 that very little substantive toxicology has been carried out on the seven candidate wood preservatives. The following recommendations are therefore made to obtain these data:

1. To provide initial toxicology data on the seven compounds, the following studies (Phase I studies) are necessary:

- a. Acute oral toxicity in rats and mice
- b. Acute dermal toxicity in rats and rabbits
- c. Eye and skin irritation in rabbits
- d. Skin sensitization in guinea pigs
- e. Ames assay in microbes

2. At the completion of the Phase I studies, the following studies (Phase II studies) are recommended:

- a. 90-day oral toxicity in rats and mice
- b. Toxicokinetics in rats and mice

The decision to undertake Phase II studies on some or all of the compounds, should be made only when the results of the field evaluation studies are available.

3. Phase III studies on selected compounds should include the following:

- a. Two-year oral toxicity in rats and mice
- b. Reproduction in rats
- c. Teratology in rats and rabbits
- d. Further metabolism in various animals

Because of the potential carcinogenicity of two of the candidate compounds (Cu-8 and TCMTB), at least these two should be evaluated for carcinogenicity by the standard bioassay in rodents.

4. Because of the various nature of the use and environmental exposures of these compounds, they will contaminate the water and soil environments. Hence, the following initial studies should be considered:

- a. Acute and chronic aquatic toxicity in fish and some other species
- b. Soil degradation and transformation into the food chain

#### LITERATURE CITED

1. HQDA, DRDAR-LCU-S-P, Letter, 27 April 1981, Subject: Request for Health and Environmental Hazards Data Support for MCI Project No. 5810976 - Nontoxic Preservative Treatments for all Wooden Army Products.
2. Environmental Protection Agency, Office of Pesticide Programs. January 1981. Wood Preservative Pesticides - Creosote, Pentachlorophenol and the Inorganic Arsenicals (Wood Uses). Position Document 2/3.
3. National Toxicology Program. Annual Plan for Fiscal Year 1981. 1980. NTP/DHHS. NTP-80-62.
4. Criteria for a Recommended Standard - Occupational Exposure to Organotin Compounds. 1976. DHEW (NIOSH) Publication No. 77-115.



## APPENDIX A

### PENTACHLOROPHENOL

A complete toxicology literature search was not initiated on PCP because the present uses of this compound are being discontinued by the U.S. Army. For comparative purposes it is being evaluated in field tests along with the seven candidate wood preservatives at the Forest Products Laboratory, Madison, WI.<sup>1</sup>

For the acute toxicity of PCP in experimental animals and fish, see the summary in the Registry of Toxic Effects of Chemical Substances, 1979.<sup>2</sup> For a review of the biological data of PCP relevant to the evaluation of its carcinogenic risk to humans, see the IARC Monographs.<sup>3</sup> Other studies, including fetotoxicity, teratogenicity, potential oncogenicity, and reproductive effects of PCP are reviewed in the EPA Position Document No. 2/3.<sup>4</sup>

### LITERATURE CITED

1. Forest Products Laboratory, Madison, WI, (USDA, Forest Service) Letter, 3 April 1981, to Dr. Jack C. Dacre, USAMBRDL, from Dr. Rodney C. DeGroot, FPL.
2. Registry of Toxic Effects of Chemical Substances, 1979 Edition. Vols. 1 and 2. 1980. R.J. Lewis, Sr. and R.L. Tatken, eds. DHHS (NIOSH) Publication No. 80-111.
3. Pentachlorophenol. 1979. IARC Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Humans 20:303-325.
4. Environmental Protection Agency, Office of Pesticides Programs. January 1981. Wood Preservative Pesticides - Creosote, Pentachlorophenol and the Inorganic Arsenicals (Wood Uses). Position Document No. 2/3.

## APPENDIX B

### COPPER NAPHTHENATE

The acute oral LD<sub>50</sub> in rats dosed with copper naphthenate (8% copper) was determined to be greater than 6.0 g/kg.<sup>1</sup> The Shell Chemical Company in an unpublished report (quoted in the Registry of Toxic Effects of Chemical Substances, 1979)<sup>2</sup> gave the lowest lethal oral dose in the mouse at 110 mg/kg. A recent report indicates that this compound is an irritant to human skin.<sup>3</sup>

### LITERATURE CITED

1. Rockhold, W.T. 1955. Toxicity of naphthenic acids and their metal salts. Arch. Indust. Hlth. 12:477-482.
2. Registry of Toxic Effects of Chemical Substances, 1979 Edition. Vols. 1 and 2. 1980. R.J. Lewis, Sr. and R.L. Tatken, eds. DHHS (NIOSH) Publication No. 80-111.
3. Wilkinson, D.S. 1979. Timber preservatives. Contact Dermatitis 5(4):278-279.

## APPENDIX C

### COPPER 8-QUINOLINOLATE

#### MAMMALIAN TOXICOLOGY

##### 1. Acute animal studies:

The LD<sub>50</sub> (95% confidence limits) in the mouse for Cu-8 administered intraperitoneally is 67 (56-80) mg/kg.<sup>1</sup> Some evidence for sex specificity (females) and delayed toxicity was also reported. An earlier study<sup>2</sup> reported the lowest toxic doses of this compound to be 156 mg/kg when administered subcutaneously in the mouse.

##### 2. Carcinogenicity studies:

Cu-8 (0.1 mg) was administered weekly by subcutaneous injection to 20 mice. After 10 months one mouse was reported as having a pleomorphic sarcoma.<sup>2</sup> Two other studies have been reported and the results summarized in the IARC Monographs.<sup>3</sup> The compound has been tested in two strains of mice both by the oral route and by single subcutaneous administration, with the effects observed for 18 months. In the latter study, a significant increase in the incidence of reticulum-cell sarcomas was observed only in the males of one strain. No evaluation of the carcinogenicity of this compound could be made on the basis of the available animal data.

##### 3. Mutagenicity study:

The compound (as the commercial product "Fennotox 45") was evaluated in the Ames bioassay (5 stains). The results were negative, i.e., no reversions at a level of 5 µg in both S-9 activated and non-activated tests.

#### LITERATURE CITED

1. Bernstein, E.H., P.W. Pienta, and H. Gershon. 1963. Acute toxicity studies on 8-quinolinol and some derivatives. Toxicol. Appl. Pharmacol. 5:599-604.
2. Haddow, A. and E.S. Horning. 1960. On the carcinogenicity of an iron-dextran complex. J. Nat. Cancer Inst. 24:109-147.
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APPENDIX D

3-iodo-2-propynyl butylcarbamate

No toxicological information was retrieved on this compound.

## APPENDIX E

### 2-(THIOCYANOMETHYLTHIO)BENZOTHAZOLE

#### MAMMALIAN TOXICOLOGY

The oral LD<sub>50</sub> of this compound for rats is given as 1,590 mg/kg in the Farm Chemicals Handbook, 1977, p. D44 (as quoted in the Registry of Toxic Effects of Chemical Substances, 1979).<sup>1</sup>

TCMTB has been reported to be mutagenic when tested by the Salmonella typhimurium system and Bacillus subtilis as test microorganisms.<sup>2</sup>

#### AQUATIC TOXICITY

The acute toxicity of TCMTB ("Busan 72") to harlequin fish (Rasbora heteromorpha Duncker)<sup>3</sup> are as follows:

LC <sub>50</sub>	0.13	24 hr (mg/L <sup>-1</sup> )
LC <sub>50</sub>	0.075	48 hr (mg/L <sup>-1</sup> )
LC <sub>50</sub>	0.036	96 hr (mg/L <sup>-1</sup> )
LC <sub>50</sub>	0.006	3 months extrapolated (mg/L <sup>-1</sup> )

The aquatic toxicity of TCMTB to some freshwater organisms (Cyprinus carpio, Oryzias latipes, Misgurnus anguillicaudatus, Daphnia pulex, D. carinata, Moina macrocopa, Indoplanorbis exustus, Cipangopaludina malleata) has been reported.<sup>4</sup> The TL<sub>m</sub> values ranged from 0.15 to >100 ppm.

#### ENVIRONMENTAL STUDY

Treatment of soil with TCMTB (50-300 ppm) had little effect on the total number of cellulolytic microorganisms; it changed the qualitative composition of the microflora by replacing Fusarium, Penicillium, Aspergillus, Trichoderma and Chaetomium species with Streptomyces; it decreased the ammonifying capacity of the soil and inhibited the soil urease enzyme activity.<sup>5</sup>

#### LITERATURE CITED

1. Registry of Toxic Effects of Chemical Substances, 1979 Edition. Vols. 1 and 2. 1980. R.J. Lewis, Sr. and R.L. Tatken, eds. DHHS (NIOSH) Publication No. 80-111.
2. Jeang, C.-L. and Li, G.-C. 1978. Screening of mutagenic pesticides using microbial systems. K'o Hsueh Fa Chan Yueh K'an. 6(8):780-788. [CA. 90:198541b, 1979].
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5. Voets, J.P. and Vandamme, E. 1970. Influence of 2-(thiocyanomethylthio)-benzothiazole on the microflora and enzymes of the soil. Meded. Fac. Landbouwwetensch., Rijksuniv. Gent. 35(2):563-580. [CA. 76:136678d, 1972].

## APPENDIX F

### ZINC NAPHTHENATE

There is only one report in the literature on the toxicity of zinc naphthenate to animals. Smyth et al.,<sup>1</sup> reported the oral LD<sub>50</sub> (95% confidence limits) for rats to be 4.92 (3.76-6.46) g/kg. A recent report indicates that this compound is an irritant to human skin.<sup>2</sup>

### LITERATURE CITED

1. Smyth, H.F., C.P. Carpenter, C.S. Weil, V.C. Pozzani, J.A. Striegel, and J.S. Nycum. 1969. Range-finding toxicity data: List VII. Am. Indust. Hyg. Assoc. J. 30:470-476.
2. Wilkinson, D.S. 1979. Timber preservatives. Contact Dermatitis 5(4):278-279.

## APPENDIX G

### AMMONIACAL COPPER BORATE

No toxicological information was retrieved on this compound. It has not been assigned a CAS Registry number. It would appear that ammoniacal copper borate is a relatively new wood preservative and was originally tested at the Forest Products Laboratory, USDA Forest Service, Madison, WI, in 1978.<sup>1</sup>

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## APPENDIX H

### TRI-n-BUTYLTIN OXIDE

#### MAMMALIAN TOXICOLOGY

##### 1. Human Exposures:

The effects of organotin compounds on humans have been summarized in the NIOSH criteria document.<sup>1</sup> TBTO was described as an irritant of the eyes, skin, and respiratory tract in employees exposed to mixtures or products containing the compound. These effects occur at air concentrations reported to be below the recommended skin TLV of 0.1 mg/cu m as tin.<sup>2</sup> A recent report also notes that TBTO is an irritant to human skin.<sup>3</sup>

##### 2. Experimental Animals:

The acute toxicity of TBTO has been determined in the rat, mouse, and rabbit by various routes of exposure. The following summary of LD<sub>50</sub>'s is from the 1979 NIOSH Registry<sup>4</sup> and other publications:

Rat:	oral	87 mg/kg	
	oral (aqueous)	194 mg/kg	Ref. 5
	oral (oil)	148 mg/kg	Ref. 5
	oral	234 mg/kg	Ref. 6
	oral	197 mg/kg	Ref. 7
	intraperitoneal	20 mg/kg	Ref. 8
	intraperitoneal	7.21 mg/kg	
	subcutaneous	11,700 mg/kg	
Mouse:	dermal	11,700 mg/kg	
	oral	55 mg/kg	
	intravenous	50.6 mg/kg	
	intraperitoneal	16 mg/kg	Ref. 8
Rabbit:	oral	50 mg/kg	(lowest lethal dose)
	dermal	900 mg/kg	
	eye	50 µg/24 hr	(severe effects)
	eye	460 µg	

TBTO produced a moderate degree of dermal irritation in the rabbit, and there were gross signs of systemic toxicity from skin absorption.<sup>5</sup> The compound was highly irritating to guinea pig skin but possessed no sensitizing properties.<sup>6</sup>

##### 3. Mutagenicity Study:

The mutagenicity of TBTO was studied in mice by measuring the number of aberrant anaphases in the bone marrow.<sup>9</sup> The 11.7% increase after 3 days following a single oral LD<sub>50</sub> dose of TBTO was significant.

##### 4. Subchronic Toxicity Studies:

When TBTO was fed to young mice for 7 days at levels of 260 µ equiv level, in addition to the loss in spleen weight and body weight, there was an alteration in the blood composition. The conclusion was that TBTO toxicity

was associated with changes in the lymphatic tissues and blood composition of mice.<sup>10</sup> Male CD rats were fed TBTO in the diet at levels of 32, 100, and 320 ppm for 30 days.<sup>5</sup> All animals showed growth suppression, which was most severe in the high dose group. Food consumption also was greatly reduced in the high dose group. Pathologic investigation revealed no effects which could be attributed to the dietary ingestion of TBTO. Similar results were reported when male rats were fed a high dose of 20 mg/kg TBTO for 4 months.<sup>11</sup>

#### AQUATIC TOXICITY STUDY

The 24 hr EC<sub>50</sub> (95% confidence limits) of TBTO for Alburnus alburnus was 0.015 (0.013-0.017) mg/L and for Nitocra spinipes was 0.002 (0.001-0.003) mg/L.<sup>13</sup>

#### ENVIRONMENTAL STUDY

The degradation of TBTO (labeled with <sup>14</sup>C) in two soils was studied under laboratory conditions. Half of the compound disappeared from unsterilized silt loam and sandy loam in ca. 15 and 20 weeks, respectively; it disappeared from the sterilized soils to a much lesser extent.<sup>14</sup> The identification of small amounts of dibutyltin derivatives and carbon dioxide in both soils confirmed the microbial participation in the degradation of TBTO.

#### ENVIRONMENTAL STANDARDS

A TLV for organic compounds of tin absorbed through the skin of 0.1 mg/m<sup>3</sup> (as tin) was set to prevent systemic toxicity.<sup>2</sup> The current federal standard (29 CFR 1910.1000) is a TWA concentration limit of 0.1 mg/m<sup>3</sup>, measured as tin. NIOSH has recently reviewed the basis for setting the previous standards and after considering all available reports on human occupational exposure and animal toxicity data to organotin compounds, recommended that the current federal standard of 0.1 mg/m<sup>3</sup>, as tin, as a TWA concentration limit be retained for all tin compounds until more definitive information has been obtained.<sup>1</sup>

#### TOXICOLOGY OF ORGANOTIN COMPOUNDS

Three reviews on the comparative toxicology and biological effects of all the organotin compounds should be consulted for further information on these compounds.<sup>15-17</sup>

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